REMARKS

The Office Action dated August 11, 2003 presents the examination of claims 1-10, 16-23 and 28-30. Claims 1 and 30 are amended. Support for the recitation of "Brassica" in claim 30 is found in the specification, such as on page 13, lines 17-19. No new matter is inserted into the application.

Rejection under 35 U.S.C. §§ 101/112, first paragraph

The Examiner rejects claims 1-10, 16-23, and 28-30 under 35 U.S.C. § 101, for an alleged lack of utility. The Examiner also rejects claims 1-10, 16-23, and 28-30 under 35 U.S.C. § 112, for an alleged lack of enablement. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Experimental data showing the function of the raffinose synthase of the present invention

First, the Examiner asserts that the specification provides no evidence which shows or suggests that the proteins encoded by the nucleic acids of the present invention actually function as raffinose synthase enzymes. In response to the Examiner's remarks, Applicants submit herewith a Declaration under 37 C.F.R. § 1.132 by

Dr. Eijiro WATANABE (an inventor of the present application) showing that the claimed nucleic acids are indeed raffinose synthase genes. An executed copy of the Declaration will follow.

As described in the Declaration, vectors containing a nucleic acid of the present invention either in the sense or antisense direction (as described in Example 8 of the instant specification) were transformed into tobacco. The raffinose synthase activity of the leaves of the transformed plants was then measured according to the procedure described on page 31, line 22 to page 33, line 9 of the specification. The results show that a higher raffinose synthase activity was found in the leaves in which the nucleic acid of the present invention was inserted in sense direction than in the leaves of the wild type plant and leaves in which the nucleic acid of the present invention was inserted in the antisense direction. As such, it is unequivocally shown that the claimed nucleic acids of the present invention express raffinose synthase activity in a transformed plant.

Therefore, the claimed nucleic acids of the present invention possess utility under 35 U.S.C. § 101. Withdrawal of the instant rejection is therefore respectfully requested.

Homology among raffinose synthase (RFS), seed imbibition protein (SIP), and stachyose synthase (STP)

Second, the Examiner relies on Peterbauer et al., *Planta* 215:839-846 (2002) to assert that raffinose synthase enzymes have a high amino acid sequence homology with seed imbibition proteins and stachyose synthases, and thusly, homology cannot be used to assert function. Applicants respectfully disagree that raffinose synthase enzymes (RFSs), seed imbibition proteins (SIPs) and stachylose synthases (STSs) cannot be distinguished from one another based upon homology.

Table 1 attached hereto shows a list of RFS, SIP, and STS proteins. Table 2 attached hereto shows the overall sequence homology (%) among the amino acid sequences of RFSs, SIPs and STSs. As shown in Table 2, homologies among RFSs, SIPs and STSs are 29-98%. However, the actual homologies between RFSs and SIPs, or RFSs and STSs are low.

For example, the homologies between RFSs and SIPs are less than 40%. Specifically, the SIP shown in Table 2 (i.e., HvSIP) has only between 29% and 39% homology with the RFSs shown in Table 2. Similarly, the homologies between RFSs and STSs are less than 45%. Specifically, the STSs shown in Table 2 (i.e., PsSTS-1, PsSTS-2, VaSTS, AmSTS, and SsSTS) all have between 35% and 44% homology with

the RFSs shown in Table 2.

On the other hand, the homologies among RFSs are all 50% or higher. For example, the homology between Sc-03 and Sc-02 is 62%, the homology between Sc-04 and Sc-02 is 54%, and so on. Thus, the homologies among RFSs are higher than those homologies between RFSs and SIPs and between RFSs and STSs. As such, contrary to the Examiner's remarks, the skilled artisan could rely on homology to determine whether or not a nucleic acid would actually encode a raffinose synthase enzyme.

Moreover, RFSs, SIPs, and STPs are phylogenetically distinguishable. A molecular phylogenetic tree of the RFSs, STSs and STSs shown in Table 1 is drawn in Figure 1 attached hereto. The molecular phylogenetic tree is drawn by the UPGMA method using the gene analysis software GENETYX-SV/RC for Windows version 6.1.0 (GENETYX Corporation; http://www.sdc.co.jp/genetyx/) and using default parameters. In the molecular phylogenetic tree, RFSs, SIPs and STSs form different groups respectively.

In summary, Table 2 and Figure 1 show that RFSs, SIPs and STSs can be easily distinguished from one another based upon a comparison of their amino acid sequences. Thus, contrary to the Examiner's remarks, amino acid sequence similarity can be used to assert function. For the above reasons, Applicants respectfully

submit that the claimed invention complies with 35 U.S.C. § 101. Withdrawal of the instant rejection is therefore respectfully requested.

Further, since the claimed invention is supported by a well-established utility under 35 U.S.C. § 101, one skilled in the art would know how to use the claimed invention. Therefore, the rejection under 35 U.S.C. § 112, first paragraph is improper and should be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph, Written Description

The Examiner maintains the rejection of claims 1, 16-23, and 28-30 under 35 U.S.C. § 112, first paragraph for an alleged lack of written description. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Description based upon homology

First, the Examiner again relies on the teachings of Peterbauer et al. to assert that one of skill in the art cannot describe a raffinose synthase based upon amino acid sequence similarity. Applicants respectfully disagree for the reasons provided above. Specifically, the homologies between raffinose synthase enzymes and

seed imbibition proteins or stachylose synthases are considerably lower than the homologies among raffinose synthase enzymes. Thus, one of skill in the art could describe a putative raffinose synthase based upon its sequence similarity with known raffinose synthase enzymes. In any event, Applicants have provided evidence in the form of a Declaration under 37 C.F.R. § 1.132 showing that the claimed nucleic acids of the present invention actually encode proteins having raffinose synthase activity.

Description based upon hybridization

Second, the Examiner asserts, "If Applicant is able to provide evidence of function of the describe [*sic*] nucleic acids, then it is the Examiner's position that the description of such nuclei [*sic*] acid does not adequately describe other nucleic acids that hybridize to said sequences as broadly claimed in claims 1 and 30."

Thus, even in the showing of actual experimental evidence, the Examiner appears to assert that the genus of nucleic acids recited in sections (i), (j), and (k) of claims 1 and 30 are not sufficiently described in the specification. Applicants respectfully disagree.

The nucleic acids recited in sections (i), (j), and (k) of claims 1 and 30 are described by: (1) origin of the nucleic acid, (2) the PCR primers utilized to obtain the nucleic acid, (3) the

ability of the nucleic acid to hybridize with a known nucleic acid under stringent hybridization conditions, and (4) the ability of the nucleic acid to encode a protein having raffinose synthase activity.

Such description is above and beyond what is required by the USPTO to meet the requirements of written description. The "Revised Interim Written Description Guidelines Training Materials" (hereinafter "the Training Materials") published by the United States Patent and Trademark Office on January 5, 2001 utilizes hybridization language to describe a genus of nucleic acids. Specifically, Example 9 of the Training Materials addresses claims that recite the invention in terms of hybridization to a reference sequence. Thus, Example 9 is relevant to the instant claims 1 and 30. The claim in Example 9 states:

> An isolated nucleic acid that specifically hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO: 1, wherein said nucleic acid encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity.

This claim language is identical in its general content to that of claims 1 and 30 in that both a reference sequence and a biological activity are set forth. The instant claims are even more delineated than the example provided by the USPTO in that the

instant claims also limit the nucleic acids to specific origins (i.e., soybean, *Chenopdiaceae*, *Cruciferae*, beet, or *Brassica*) and are obtained by the use of specific primers pairs (i.e., SEQ ID NOs: 9 and 10, SEQ ID NOs: 11 or 13 and 12 or 14, SEQ ID NOs: 12 and 14, and SEQ ID NOs: 15, 17, or 19 and 16, 18, or 20).

The disclosure in the instant specification is also above and beyond what is required by the USPTO and exemplified in Example 9. Specifically, in Example 9, there is only **one** cDNA disclosed that encodes a protein that has the biological activity recited in the claims. In contrast, the instant specification describes **a plurality** of isolated nucleic acids which encode raffinose synthase (SEQ ID NOs: 2, 4, 6, and 8). In any event, the USPTO considers that the disclosure of **one** species within the genus is sufficient: "Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention." See, Training Materials, pages 36-37. Therefore, the instant disclosure of **a plurality** of isolated nucleic acids certainly is adequate to describe the genus of nucleic acids encompassed by claims 1 and 30.

For all of the above reasons, Applicants respectfully submit

that the pending claims are fully described in the specification such that the requirements of 35 U.S.C. § 112, first paragraph are met. Withdrawal of the instant rejection is therefore respectfully requested.

Rejection under 35 U.S.C. § 112, first paragraph, Enablement

The Examiner maintains the rejection of claims 1-10, 16-23, and 28-30 under 35 U.S.C. § 112, first paragraph for an alleged lack of enablement. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Function based upon homology

Again, the Examiner again relies on the teachings of Peterbauer et al. to assert that one of skill in the art cannot assume the function of a raffinose synthase based upon amino acid sequence similarity. Again, Applicants respectfully disagree for the reasons provided above. Specifically, the homologies between raffinose synthase enzymes and seed imbibition proteins or stachylose synthases are considerably lower than the homologies among raffinose synthase enzymes. Thus, one of skill in the art could predict the function of a nucleic acid based upon its sequence similarity with known raffinose synthase enzymes.

Undue experimentation

The Examiner also argues that it would require undue trial and error experimentation by one of skill in the art to make and use the genus of nucleic acids claimed and confirm their function. Applicants strongly disagree.

First, the Examiner is reminded, "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation." U.S. Pat. & Trademark Off., *Manual Pat. Examining Proc.* § 2164.01 (8th ed. rev. 1, 2003). Second, the Examiner is reminded that the Federal Circuit has also held that a specification was enabling when "there was considerable direction and guidance" in the specification; there was "a high level of skill in the art at the time the application was filed"; and "all of the methods needed to practice the invention were well known." In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988).

In the present case, there is a high level of skill in the art (e.g., a Ph.D. in biochemistry or its equivalent), the specification provides considerable direction and guidance (as described below), and all of the methods needed to practice the invention are known (as described below). Thus, it would not cause the skilled artisan undue experimentation to make or use the

claimed nucleic acids of the present invention.

(a) Guidance in the specification

The instant specification provides PCR primers and a detailed description of how to use them to isolate additional examples of nucleic acids encoding raffinose synthase. Working examples 1-7 show the use of the PCR primers to perform such isolations. This disclosure is much more than a "mere statement that [broadly claimed DNA] is part of the invention and reference to a potential method of isolating it." Fiers v. Sugano, 25 USPQ2d 1601 (Fed. Cir. 1993). This disclosure constitutes actual variants within the claimed genus and actual methods that can be used to find the next species within the genus. The specification further provides a detailed description of an assay that can be used to determine if the protein encoded by an isolated nucleic acid is in fact a functional raffinose synthase. Specifically, page 31, line 22 to page 33, line 9 of the specification discloses detailed instructions for measuring raffinose synthase activity. This method was also utilized in the Declaration under 37 C.F.R. § 1.132.

(b) All of the methods needed to practice the invention are known

All of the methods need to practice the present invention are

readily known by the skilled artisan. For example, section (i) of claim 1 is directed to a nucleotide sequence obtained from a polynucleotide which is amplified from a nucleic acid obtained from soybean with a combination of a PCR primer of SEQ ID NO: 9 and a PCR primer of SEQ ID NO: 10, wherein said nucleotide sequence hybridizes with a nucleotide sequence complementary to the nucleotide sequence of (a) or (b), in a buffer comprising 0.9M NaCl and 0.09M citric acid at 65°C to 68°C. Thus, the methods needed to obtain such a nucleic acid include DNA isolation from soybean, PCR amplification using specific primers, and hybridization. It is uncontestable that all of these techniques are widely utilized such that their use is routine the art.

For example, genomic libraries and PCR primers are commercially available. Automated machines can complete hundreds of PCR reactions at a time, such that the entire genus of plants could be screened within days. Thus, even if the genus of plants is large, it would not cause the skilled artisan undue experimentation to screen the genus via PCR.

In summary, considering that there is a high level of skill in the art (e.g., a Ph.D. in biochemistry or its equivalent) and that all of the methods needed to practice the invention are known and provided for in the specification (e.g., PCR and raffinose synthase

activity assay), it would not be undue experimentation to make or use the claimed nucleic acids of the present invention. The instant rejection is therefore improper and should be withdrawn.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejects claims 1, 16-23, and 28-30 under 35 U.S.C. § 112, second paragraph for allegedly being indefinite. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Specifically, the Examiner asserts that the phrases "obtainable," "hybridizable," and "amplifiable" in claims 1 and 30 are unclear. In response to the Examiner's remarks, Applicants amend these terms into past tense.

Applicants respectfully submit that the instant claims particularly point out and distinctly claim the subject matter that is the present invention such that the requirements of 35 U.S.C. § 112, second paragraph are met. Withdrawal of the instant rejection is therefore respectfully requested.

Conclusion

Applicants respectfully submit that the above remarks and/or amendments fully address and overcome the rejections of record. The present application is in condition for allowance. The Examiner is respectfully requested to issue a Notice of Allowance indicating that claims 1-10, 16-23, and 28-30 are allowed.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. 45,702) at the telephone number of the undersigned below.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of three (3) months to February 11, 2004, in which to file a reply to the Office Action. The required fee of $950.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees

required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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GMM/KLR:gmh
0020-4559P

Attachments: Table 1: List of RFS, SIP, and STS enzymes
Table 2: Homologies (%) among RFS, SIP, and STS enzymes
Figure 1: Phylogenetic tree of RFS, SIP, and STS enzymes
Declaration under 37 C.F.R. § 1.132

Table 1

Code	Protein*	Organism	Accession**	Reference	Author/Assignee
Sc-03	RFS	***Beta vulgaris***	E37133	09/301,766	Sumitomo Chemical
Sc-05	RFS	***Brassica juncea***	E36417	09/301,766	Sumitomo Chemical
Sc-02	RFS	***Vicia faba***	E24423	08/992,914	Sumitomo Chemical
Sc-04	RFS	***Glycine max***	E24424	08/992,914	Sumitomo Chemical
Aj-05	RFS	***Cucumis sativus***	AF073744	Family GH36***	Ohsumi et al.
PsRFS	RFS	***Pisum sativum***	AJ426475	Family GH36	Peterbauer et al.
HvSIP	SIP	***Hordeum vulgare***	M77475	Family GH36	Heck et al.
PsSTS-1	STS	***Pisum sativum***	AJ311087	Family GH36	Peterbauer et al.
PsSTS-2	STS	***Pisum sativum***	AJ512932	Family GH36	Peterbauer et al.
VaSTS	STS	***Vigna angularis***	Y19024	Family GH36	Peterbauer et al.
AmSTS	STS	***Alonsoa meridionalis***	AJ487030	Family GH36	Voitsekhovskaja
SsSTS	STS	***Stachys affinis***	AJ344091	Family GH36	Pesch and Schmitz

*Protein: RFS, Raffinose synthase; SIP, Seed Imbibition Protein; STS, Stachyose synthase.

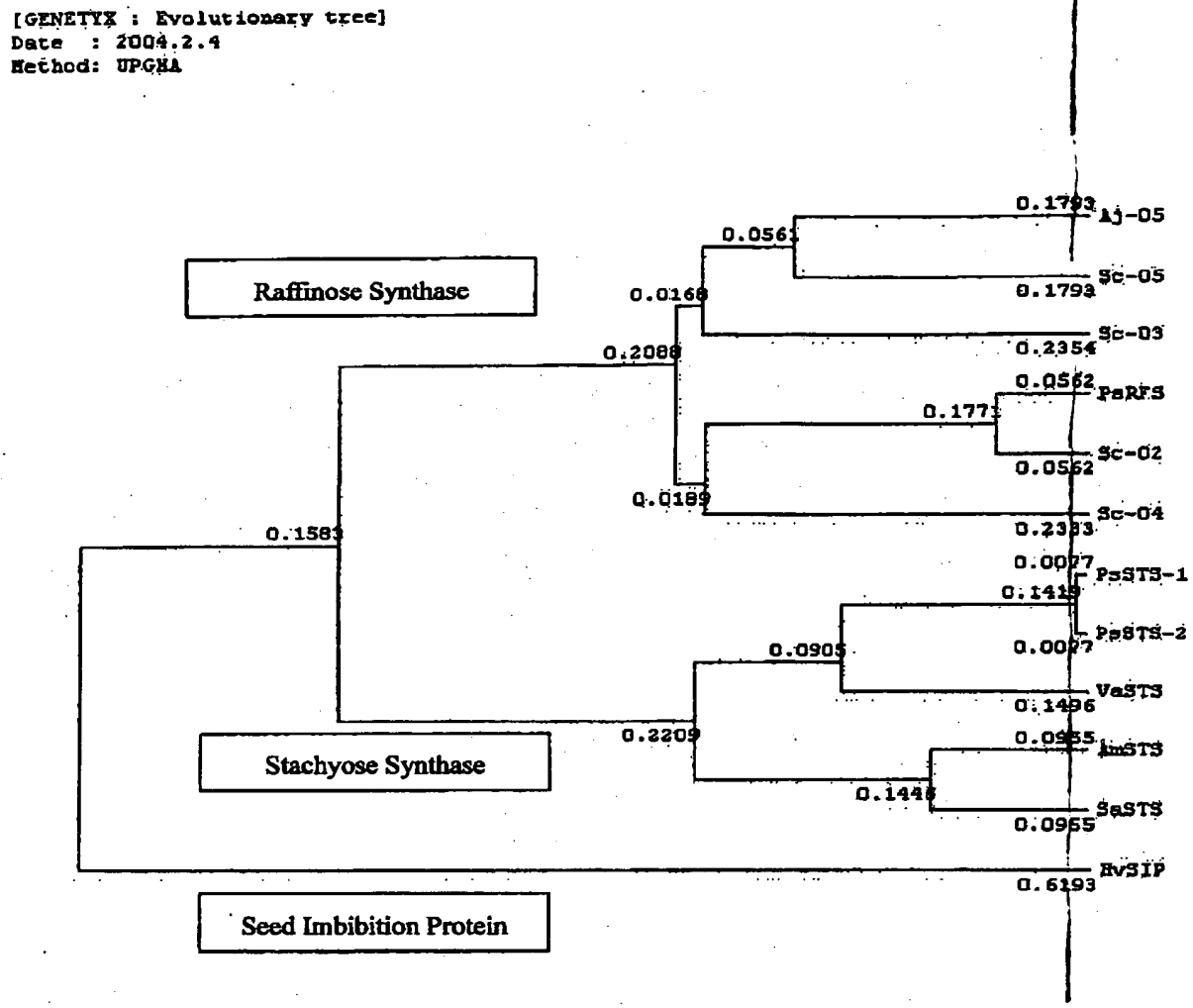
**Accession: GenBank Accession Number.

***Family GH36: glycoside hydrolase family 36 (see Carbohydrate-Active Enzymes (CAZy) database: http://afmb.cnrs-mrs.fr/CAZY/GH_36.html)

Table 2

Code	Sc-02	Sc-03	Sc-04	Sc-05	PsRFS	Aj-05	HvSIP	AmSTS	PsSTS-1	PsSTS-2	SaSTS	VaSTS
amino acids	800	783	611	777	798	784	757	868	853	847	863	857
Sc-02		62	54	62	89	64	39	43	43	42	42	43
Sc-03			50	63	63	66	39	42	43	42	42	43
Sc-04				50	54	50	29	35	35	35	34	36
Sc-05					62	70	39	44	44	43	44	45
PsRFS						64	38	42	43	43	42	43
Aj-05							38	42	44	43	43	43
HvSIP								33	34	34	34	34
AmSTS									64	64	83	64
PsSTS-1										98	65	75
PsSTS-2											65	74
SaSTS												65
VaSTS												

Fig. 1


[GENETYX : Evolutionary tree]
Date : 2004.2.4
Method: UPGMA
Raffinose Synthase
Stachyose Synthase
Seed Imbibition Protein
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Aj-05
0.0561
Sc-05
0.1793
0.0168
Sc-03
0.2354
0.2088
0.0562
PsRFS
0.1771
Sc-02
0.0562
0.0189
Sc-04
0.2383
0.1581
0.0077
PsSTS-1
0.1419
PsSTS-2
0.0077
0.0905
VaSTS
0.1496
0.2209
0.0965
AmSTS
0.1448
SaSTS
0.0965
RvSIP
0.6193